

### **REMARKS/ARGUMENTS**

Claims 1-40 were in the original application; following a restriction requirement, claims 1-34 were elected and claims 35-40 withdrawn from consideration; claims 1-34 have been rejected.

Claims 1-26 and 34 are rejected under 35 USC § 112, second paragraph, as being indefinite.

a. Claim 1 has been amended to make it clear that the composition comprises the two components.

b. Claim 2 has been amended as suggested by the Examiner.

c. Claim 2 has been further amended to relate the composition to the substrate.

d. Claim 4 has been amended as suggested by the Examiner.

e. & f. Claims 5 and 6 have been amended as suggested by the Examiner.

g. Claim 25 has been canceled.

h. Claim 34 has been amended to depend from claim 27 instead of claim 25.

The Applicant believes that the amended claims are now in compliance with 35 USC § 112, second paragraph, and that the rejection should be withdrawn.

### ***Claim Rejections Under 35 USC § 102***

Claims 1-11, 15-24, 27-29 and 31-34 have been rejected under 35 USC § 102(b) as being anticipated by Walt et al (WO 00/16101, published 23 March 2000). This rejection is respectfully traversed.

In his rejection, the Examiner has referred to page 22, lines 9-22 and page 7, line 14 of the application of Walt et al. (WO 00/16101). The following is an excerpt from lines 9-22:

*The micro-spheres are then placed in the wells 250 in step 276 according to a number of different techniques. The placement of micro-spheres may be accomplished by dripping a solution containing the desired randomly mixed subpopulations of the micro-spheres over the distal end 212, sonicating the bundle to settle the micro-spheres in the wells, and allowing the micro-sphere solvent to evaporate. Alternatively, the subpopulations could be added serially to the bundle end. Micro-spheres 10 may then be fixed into the wells 250 by using a*

*dilute solution of sulfonated Nafion that is dripped over the end. Upon solvent evaporation, a thin film of Nafion was formed over the micro-spheres which holds them in place.*

It is clearly stated that the surface contains wells and the micro-spheres are settled in the wells before the solvent is evaporated. Immobilization is achieved by settling the micro-spheres in the wells prior to evaporation of the solvent and not by a sol-gel transition in the medium. The micro-spheres may be further fixed in place by using a film-forming polymer. The material Nafion is a film-forming fluoropolymer sold by DuPont that is insoluble in water. It is not a gelling agent, as stated by the Examiner. Information on Nafion is enclosed with this response.

With reference to page 7, line 14; the word 'planar' as used by Walt et al. does not indicate an absence of specific sites capable of interacting with the micro-spheres as stated by the Examiner. The term is used to distinguish a two-dimensional configuration from a three-dimensional configuration (lines 15 and 16). It is clearly stated on page 7, lines 3-5 that:

*'substrate' or 'solid support' or other grammatical equivalents herein is meant any material that can be modified to contain discrete individual sites appropriate for the attachment or association of beads ....*

Again on line 21 of the same page: *"At least one surface of the substrate is modified to contain discrete, individual sites for later association of micro-spheres".*

Walt et al. and the Applicant have used different approaches as discussed above. In an attempt to graphically show the differences, the Applicant has included diagrams depicting the invention and the prior art. The rejection should be withdrawn.

Claims 1-8, 12-13,24 and 27-34 have been rejected under 35 USC § 102(e) as being anticipated by Anderson et al (U.S. Patent Application Publication No. 2002/0015952, filed 1 February 2001). This rejection is respectfully traversed.

Anderson et al. (U.S. Patent Application No. 2002/0015952) discloses a method of preparing a micro-array wherein micro-spheres with attached biological probes are dispersed in a gelling agent such as gelatin. The composition in a fluid (sol) state is sucked into a bundle of tubules (approx. 1mm internal diameter) and allowed to chill set (sol-gel transition). The bundle of tubules is then cross-sectioned using a micro-tome and attached to a plane surface (having no preselected sites) to form an array of discs having a thickness of about 5 to 20 microns. The material making up the walls of the tubules may be selectively removed leaving behind a group of 'islands' or 'pillars' on the surface.

The application does not teach spreading the micro-spheres uniformly on the surface in the fluid state prior to immobilization via a sol to gel transition of the medium. It teaches creating structures having *three-dimensional form* (# 142) or *small pillars with a gap between them* (#143). In one embodiment cited by the Examiner (#134) it is possible to directly transfer material to a surface to create these 'pillars'. However, the material is transferred "*as a paste or a gel that remains firm or quickly hardens after being extruded onto a solid phase*". Again, in (#145) it is stated that:

*other techniques for producing a three-dimensional structure include depositing a three-dimensional structure directly on the solid surface. This may involve a preformed structure of a fluid or semi-fluid material which solidifies very quickly before it spreads significantly....*

Anderson et al. clearly teaches away from creating first a uniform spread layer of micro-spheres on the surface using coating aids or spreading agents as disclosed in Example 1 of the present application. Uniformity of coating of the micro-spheres is emphasized again in Example 2. To emphasize this difference, the Applicant has amended claim 1 to include a coating aid as shown in the examples. The cited references, Walt et al. and Anderson et al. do not use coating aids because they are not spreading, in fact do not want spreading, of the composition on the substrate. The rejection should be withdrawn.

#### ***Claim Rejections Under 35 USC § 103(a)***

Claims 12-14 and 30 have been rejected under 35 USC § 103(a) as being unpatentable over Walt et al (WO 00/16101, published 23 March 2000) in

view of Anderson et al (U.S. Patent Application Publication No. 2002/0015952, filed 1 February 2001).

Regarding Claim 12, the Examiner argues that it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the gelatin gelling agent of Anderson et al. to the gelling agent of Walt et al. to thereby use a gelling agent which gels at ambient temperature for the obvious benefits of convenience and simplicity of gelling. The rejection is respectfully traversed.

The references give no motivation or teaching for the Applicant to combine the references as the Examiner argues. As stated earlier, Walt et al. applies a thin film of Nafion over the micro-spheres to hold them in place after they were in the wells. Anderson et al. needs a material to make a three-dimensional structure before it is positioned on a substrate; the material is required to be fluid or semi-fluid, but it must solidify very quickly before it spreads significantly. The fact that gelatin is used for this purpose provides no motivation for Walt et al. to use gelatin. And even if gelatin were used by Walt et al., one would still not arrive at the present invention where the gelatin must be evenly coatable, allowing the micro-spheres to spread and form a random pattern on the substrate. Hence, a coating aid is used in the composition.

Regarding Claim 13, the Examiner contends that one of ordinary skill in the art would have been motivated to apply the thermal gelation of Anderson et al. to create a microarray because this method would simplify microarray production by eliminating the need for micro-scaled tools. Therefore, it would have been obvious to one of ordinary skill in the art to apply the thermal gelation of Anderson et al. to the gelling of Walt et al. for the expected benefit of simplifying microarray production.

Again, there is no motivation given by the references. The Applicant has no concerns about micro-scaled tools; and the Applicant is dealing with biological material that might be sensitive to heat.

Regarding Claim 14, the Examiner argues that it would have been obvious to one of ordinary skill in the art at the time the claimed invention was

made to modify the gelling agent of Walt et al. by alkali pretreating the gelling agent as claimed based on the interaction to be detected for the obvious benefit of facilitating binding of the agents of interest as taught by Anderson et al (§ 54).

The response with respect to claim 12 is reiterated here. Alkali pretreatment treatment of the gelatin does not render the claim obvious. In any case, the Applicant maintains that the composition of the invention is novel based on other factors (e.g., the coating aid; e.g., the ability for the microspheres to spread randomly on the substrate) and even if the gelatin were alkali pre-treated, the claims would still be novel.

Regarding Claim 30, the Examiner argues that it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the gelatin gelling agent of Anderson et al to the gelling agent of Walt et al. to thereby use a gelling agent which gels at ambient temperature for the obvious benefits of convenience and simplicity of gelling.

For reasons already discussed above, the instant invention remains distinguishable over Walt et al., even if Walt et al. were motivated to use the gelatin go Anderson et al.

Claim 25 is rejected under 35 USC § 103(a) as being unpatentable over Walt et al (a) (WO 00/16101, published 23 March 2000) in view of Walt et al (b) (U.S. Patent Application Publication No. 2002/0172716 A1, filed 25 October 2000).

Claim 25 has be canceled and so the rejection is now moot.

Claim 26 is rejected under 103(a) as being unpatentable over Walt et al. (WO 00/16101, published 23 March 2000) in view of Chang et al (U.S. Patent No. 4,873,102, issued 10 October 1989).

Regarding Claim 26, the Examiner argues that it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the emulsion polymerization of Chang et al. to the microspheres of Walt et al. to thereby provide microspheres of a uniform size as taught by Chang et al. (Column 6, lines 26-28) for the obvious benefits of providing consistent

microsphere surface area for surface interaction and thereby controlling interaction uniformity.

The Applicant maintains that claim novelty does not depend on having the microspheres of uniform size. The bases for novelty are as discussed at length above.

In summary, the composition and the micro-array of the invention are fundamentally different from the prior art cited by the Examiner and the enclosed drawings demonstrate this. The rejections should be withdrawn.

In view of the foregoing amendments and remarks, reconsideration of this patent application is respectfully requested. A prompt and favorable action by the Examiner is earnestly solicited. Should the Examiner believe any remaining issues may be resolved via a telephone interview, the Examiner is encouraged to contact Applicants' representative at the number below to discuss such issues.

Respectfully submitted,



---

Attorney for Applicants  
Registration No. 34,278

Doreen M. Wells/ct  
Rochester, NY 14650  
Telephone: (585) 588-2405  
Facsimile: (585) 477-1148